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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,756	CHIARI ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2005 and 11 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,15,52,54,65,66 and 72-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7,15,52,54,65,66 and 72-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a rule 371 continuation of PCT Serial Number PCT/US00/04326, which claims the benefit of the filing date of provisional applications 60/160,374 and 60/179,570.

Claims 3, 6, 8-14, 16-20, 22-51, 53, 55-64, and 67-70 have been canceled.

New claims 77-90 have been added.

Claims 1, 2, 4, 5, 15, 21, 52, 54, 65-66, and 71-90 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's amendment filed May 26, 2005 no outstanding grounds of rejection are maintained.

The following represent NEW GROUNDS of rejection, necessitating that this Office Action be made NON-FINAL.

Claim Objections

1. Claims 66 and 81 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 66 and 81 each recite that the amino acid sequence of the base claim contains D-amino acid residues. However, there are no D-amino acid residues noted in the sequence listing as being incorporated into any of the recited sequences. Therefore, the sequences of SEQ ID NOs: 3, 5, 7 and 53 as recited in the base claims comprise only L-amino acid residues. It is suggested that the recitations of D-amino acid residues be placed in independent claims reciting the replacement of amino acid residues with D-amino acid residues.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 21, 72-74, and 84-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for HLA-DR11^{+} antigen presenting cells and a method of enriching T cells that specifically bind to an epitope of EphA3 comprising SEQ ID NO: 53 or 62, does not reasonably provide enablement for antigen presenting cells or enriching T cells specific for other regions of EphA3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are most broadly drawn to a method for enriching T cells reactive with an isolated polypeptide comprising the EphA3 HLA class II binding peptide of SEQ ID NO: 53 or 62. There is no requirement that the antigen presenting cells bind to are specific for the epitope defined by the fragment of EphA3 disclosed as SEQ ID NO: 53 or 62, only that the antigen presenting cells bind to a polypeptide comprising said epitope. Similarly, there is no requirement in the claims that the T cells being enriched are specific for the epitope of SEQ ID NO: 53 or 62 presented in the context of HLA-DR11, only that the enriched T cells are reactive with the polypeptide comprising the epitope. The metes and bounds of the claims, therefore, are inclusive of antigen presenting cells and T cells that are specific not only for the EphA3 epitopes that have SEQ ID NO: 53 or 62 as their core sequence, but also of antigen presenting cells and T cells that are reactive with ANY potential epitope of EphA3 or with ANY epitope of a potential fusion partner of fragments comprising the SEQ ID NO: 53 or 62 core sequence. The specification does not provide any guidance regarding additional epitopes of the EphA3 polypeptides, nor does the specification disclose the HLA class II haplotype that would bind any additional epitopes for presentation to T cells in an HLA class II specific manner. Additionally, the specification does not disclose any information regarding epitopes of potential fusion partner polypeptide sequences that are unquestionable encompassed by the scope of the claims. The specification does not provide guidance regarding the identification of antigen presenting cells or T cells reactive with other regions of EphA3, nor does the specification provide guidance regarding how to use cells reactive with fusion partner polypeptides.

3. Claims 1, 4, 5, 7, 15, 21, 52, 54, 65, 66 and 71-90 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are most broadly drawn to polypeptides comprising a fragment of SEQ ID NO: 3, 5, or 7 containing an HLA class II binding peptide having a core sequence of SEQ ID NO: 53, nucleic acids encoding the polypeptide, antigen presenting cells comprising the polypeptide in association with HLA class II molecules and a method of enriching T cells using the polypeptide. The claims encompass any polypeptide/nucleic acid that contains the recited fragment. However, the specification only teaches three polypeptides that comprise the Eph3A HLA class II binding fragment comprising the core sequence of SEQ ID NO: 53 (which is contained within each of SEQ ID NOs: 51, 54 and 62), and those are the polypeptides disclosed in the instant specification as SEQ ID NOs: 3, 5 and 7. The specification does not teach the possession of any other polypeptide sequence comprising said core sequence.

> The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115). In the instant case, the specification does not describe the sequence of any polypeptide other than SEQ ID NO: 3, 5 or 7 that comprises the core EphA3 sequence defined by SEQ ID NO: 53. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, ((CAFC, 1991) 18 USPQ2d 1016).

Consequently, Applicant was not in possession of the instant claimed invention. See *Regents of*

the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." *Id.* 43 USPQ2d at 1404 (quoting *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention."

With the exception of SEQ ID NOs: 3, 5 and 7, the skilled artisan cannot envision the structure of any polypeptide comprising the EphA3 HLA class II-binding core sequence of SEQ ID NO: 53 and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying the peptides. Adequate written description requires more than a mere statement that it is part of the invention and a reference to antibodies which penetrate cells (page 9, lines 14-35 of the instant specification. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,((CAFC, 1991) 18 USPQ2d 1016).
Therefore, the only polypeptides adequately described to meet the written description provision of 35 USC 112, first paragraph are those that consist of a fragment of a sequence selected from the group consisting of SEQ ID NOs: 3, 5 and 7 and comprise the EphA3 HLA class II-binding peptide of SEQ ID NO: 51, 53, 54 or 62.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 7, 66 and 80-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "the isolated polypeptide is non-hydrolyzable." There is insufficient antecedent basis for this limitation in the claim. The base claims are drawn to peptides listed in the sequence listing as being composed entirely of L-amino acids. The sequences disclosed as SEQ ID NO:

3, 5, 7, 51, 53, 54 and 62 in the sequence listing do not comprise any non-hydrolyzable residues. It is suggested that claims 7 and 80 be re-drafted as independent claims reciting that residues of said sequences have been replaced with non-hydrolyzable residues.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 4, 71, 77 rejected under 35 U.S.C. 102(b) as being anticipated by Fox et al (Oncogene [1995] 10:897-905; U on form PTO-892, newly cited).

Given their broadest reasonable interpretation, the claims are broadly drawn to an isolated polypeptide comprising an EphA3 HLA class II-binding peptide fragment. The term "comprising" is an open term that is inclusive of any polypeptide that contains the fragment, up to and including the full-length protein. It is noted that the term "EphA3" is a newer, standardized, nomenclature for a protein previously known in the art as "human EPH-like Kinase," "HEK" or "HEK4."

Fox teaches the isolation of EphA3 (HEK4) cDNA from a fetal brain library and the deduced amino acid sequence therefrom (see entire reference, Figure 1a-b in particular). The HER4 sequence comprises the HLA class II binding peptide fragment of SEQ ID NO: 3, 5, or 7 that comprises SEQ ID NO: 53, 51, 54 or 62 (page 900, right end of 4th alignment group of Figure 1a in particular). Claim 2 is included because Fox teaches a 25 amino acid signal peptide that is removed, yielding a fragment of SEQ ID NO: 3, 5 or 7. The prior art teaching anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 54, 76, 89 and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al (Oncogene [1995] 10:897-905; U on form PTO-892, newly cited) as applied to claims 1 and 77 above, and further in view of Campbell (Monoclonal Antibody Technology [1985] pages 1-32; U on form PTO-892, newly cited).

Claims 54 and 89 recite a vaccine composition. A vaccine is a composition that can reasonably interpreted as comprising an immunogen and a pharmaceutically acceptable carrier.

Fox has been discussed supra. Fox does not teach monoclonal antibodies to a EphA3 polypeptide comprising SEQ ID NO: 53 or 62. Campbell teaches that "[i]t is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)" (page 29, section "Basic research" in particular). It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to make antibodies specific for EphA3 polypeptides comprising the HLA class II binding peptide segment of SEQ ID NO: 53 or 62. One would have been motivated, with a reasonable expectation of success, to generate mAbs to the peptides based on the fact that it is a conventional practice in the art to do so for further study, characterization and identification of a specific peptide and because of the potential role of the EphA3 protein as taught by Fox. Claims 76 and 90 are included because the use of an adjuvant is conventional in the art in immunization protocols.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
April 17, 2006

David A Saunders

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